

Serial No 09/852,445

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Docket No. 2598-4004US1

Amendments to the Specification:

Please replace the paragraph beginning at page 9, line 32, with the following rewritten paragraph:

--Present databases and computers allow rapid searches for partners based on surrogate sequences. Examples of available computer based programs to analyse sequences include BLAST, Patternfind, ExPASy, MEME (Multiple EM for Motif Elicitation), (<http://meme.sdsc.edu/meme/website/intro.html>) MAST (Motif Alignment and Search Tool), ([http://meme.sdsc.edu/meme/website/mast\\_intro.html](http://meme.sdsc.edu/meme/website/mast_intro.html)), ([www.expasy.ch/](http://www.expasy.ch/)) and ISREC ([www.isrec.sib.sib.ch/software/software.html](http://isrec.sib.sib.ch/software/software.html)). Identification of surrogates provides tools for partner identification, phenotyping and small molecule discovery. Given that a site directed assay is available at this early stage for the unknown target, high throughput screening allows the rapid identification of reactive small molecules of low target affinity. Combinatorial chemistry allows for improvements in potency which would then provide small molecules for phenotyping and testing in animal studies.--

Please replace the paragraph beginning at page 11, line 11, with the following rewritten paragraph:

--After identification of a surrogate peptide binder, it is subjected to partner analysis using several different database search programs. In addition, the set of multiple surrogate peptide binders are aligned into groups based on motifs or consensus regions. Motifs and consensus regions can be identified by sequence alignment programs like MEME (Multiple EM for Motif Elicitation), (<http://meme.sdsc.edu/meme/website/intro.html>). The motifs and consensus regions can be used as query patterns to search the available databases using MAST (Motif Alignment and Search Tool, [http://meme.sdsc.edu/meme/website/mast\\_intro.html](http://meme.sdsc.edu/meme/website/mast_intro.html)) or Patternfind. The identified sequences can be further examined for significant differences in the expected frequency of amino acids and the number of times a specific peptide sequence has been repeated.--

Please replace the paragraph beginning at page 11, line 28, with the following rewritten paragraph:

--In the initial step, the entire peptide sequence and consensus motifs (if found) are entered into an Advanced BLAST search (<http://www.ncbi.nlm.nih.gov/blast/blast.cgi?form=1>), using the following parameters:--

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Please replace the paragraph beginning at page 19, line 3, with the following rewritten paragraph:

--DNA fragments coding for peptides containing 40 random amino acids were generated by a PCR approach using synthetic oligonucleotides. A 145 base oligonucleotide was synthesized containing the sequence (NNK)<sub>40</sub> where N = A, C, T, or G and K = G or T. See U. S. Patents 6,143,531, and 5,681,726 and 388, which are hereby incorporated by reference. This oligonucleotide was used as the template in PCR reactions along with two shorter oligonucleotide primers, both of which are biotinylated at their 5' ends. The resulting 190 bp product was purified and concentrated (followed by digestion with SfiI and NotI). The resulting 150 bp fragment was purified and the phagemid pCANTAB5E (Pharmacia) was digested with SfiI and NotI. The digested DNA was resolved using a 1% agarose gel, excised and purified by QIAEX II treatment (Qiagen). The vector and insert were ligated overnight at 15°C. The ligation product was purified. Electrocompetent cells were prepared by harvesting cells from a culture broth with an OD of 0.5-0.7 U<sub>OD</sub> by centrifugation in a fixed rotor for 10 minutes at 950g. The cells were washed three times with ice cold pure water. Electroporations were performed at 1500 V in an electroporation cuvette (0.1 mm gap; 0.5 ml volume) containing 12.5 ug DNA and 500 uL of E. coli strain TG1 electrocompetent cells. Immediately after the pulse, 12.5 ml of pre-warmed (42°C) 2x YT medium containing 2% glucose (YT-G) was added and the transformants grown at 37°C for one hour. Cell transformants were pooled, the volume measured and an aliquot plated onto 2x YT-G containing 100 µg/ml ampicillin (YT-AG) to determine the number of transformants. The diversity of the random 40-mer peptide cell library was found to be > 1.6 X 10<sup>10</sup>. The phage library was produced by rescue of the cell library according to standard phage preparation protocols. See e.g., Carcamo, et al. Proc. Natl Acad Sci USA (1998) 95: 11146-11151. Phage titers were usually 4 X 10<sup>13</sup> CFU/ml.--